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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/646,396	08/21/2003	Donna Shattuck	1309.05	9664

26698 7590 08/15/2005

MYRIAD GENETICS INC.
INTELLECUTAL PROPERTY DEPARTMENT
320 WAKARA WAY
SALT LAKE CITY, UT 84108

EXAMINER	
CARLSON, KAREN C	
ART UNIT	**PAPER NUMBER**
1653	

DATE MAILED: 08/15/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/646,396	SHATTUCK ET AL.	
	Examiner	Art Unit	
	Karen Cochrane Carlson, Ph.D.	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 June 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *1-12 and 18-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

This Office Action is in response to the paper filed June 29, 2005.

Claims 1-12 and 18-20 are withdrawn from further consideration by the Examiner because these claims are drawn to non-elected inventions. Claims 13-17 and 21are currently under examination.

Priority is set to August 21, 2002.

Withdrawal of Objections:

The objection to the disclosure is withdrawn.

Maintenance of Rejections:

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 13-17 and new Claim 21 are again rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In Claim 13, the biological activity is not set forth and is therefore indefinite regarding what activity will be screened. It is not clear if the homolog is the mutant form of APAF1, or if the homolog has a mutation corresponding to that in APAF1? And how would one tell the difference? It is not clear if the derivative or the fragment comprise the mutation in the APAF1 or, for example, can the fragment of a mutated APAF1 be the same as a fragment for wild type, ie not having the mutation regardless of the origin of the fragment? **Additionally**, as amended, it is not clear which depression model is being used. See also Claims 14-17 and 21.

Applicants refer to the specification and state that they have identified mutants of APAF1 that are associated with depression. As noted, the claims are not written to limit the mutants, homologs, derivatives, etc. to any mutant of APAF1 having a specific activity. The cited art of record shows that different mutants increase or decrease the activity of APAF1. If a mutant decreases the activity of APAF1, then how can it be associated with depression? How could the drug candidate be useful for treating depression? While Applicants may desire breadth, the claims are so broad that they are indefinite.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 13-17 and new Claim 21are again rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification describes drug screening at pages 25-37. The specification does not describe mutant APAF1, homologues, derivatives, or fragments thereof having activity, or an activity that could be blocked that would aid in the treatment of depression. Focusing only on the mutant APAF1, this mutant APAF1 would have to maintain its wild-type biological activity – which mutations would be expected to maintain wild-type biological activity? The dependent claims list several mutations, but nowhere in the specification has the activity of these mutant APAF1 polypeptides been explored. See the Art of Record below wherein some mutations increase while others decrease the binding of APAF1 to procaspase-9, for example. Further, which activity is being assessed? That is, APAF1 interaction, with itself, cytochrome c, or caspase

-9, for example. Thus, the specification fails to provide written description of a drug screening method using mutant APAF1. The same can be said about homologues comprising this mutation, derivatives comprising this mutation, or fragments comprising this mutation.

Applicants urge that the specification describes mutant APAF1 (homologues, derivatives or fragments) that have activity and that can be blocked Again, none of these mutants have been used in the method claimed. This is why the specification lacks written description, that is, there is no description of a mutant APAF1 (etc) that has been shown to be useful in the method claimed.

Art of Record (presented again):

Mutations within APAF1 are found in the prior art; however, these mutations were used to find the interface between APAF1 and other polypeptides, such as caspase.

Yakovlev et al. (Oct. 1, 2001; J. Neuroscience 21(19): 7439-7446) teach APAF1 having mutations at Cys450Arg and Glu625Gln.

Qin et al. (1999; Nature 399:549-557) generated 20 mutations on the surfaces of APAF1 CARD domain and the procaspase-9 prodomain and found that two mutations in the APAF-1 CARD domain Asp27Ala and Glu40Ala eliminated interaction with procaspase-9 prodomain. Six mutations at Arg13, Lys42, Lys58, and Lys62 did not effect complex formation with procaspase-9.

Walke et al. (2000; Brain Res. 886:73-81) teach a murine variant of APAF1 having an 11 amino acid insert named APAF-1L. Both bind caspase 9, and unlike the C-elegans homolog CED-4, neither variant was lethal in yeast. APAF1L was more potent than APAF1.

Hu et al. (1999; EMBO J. 18(13): 3586-3595) show that APAF1 having Met368Leu could activate procaspase-9 while the conservatively substituted APAF1 having Lys160Arg could not.

Day et al. (1999; Cell Death and Differentiation 6:1125-1132) used alanine scanning mutatgenesis to demonstrate that mutations at K42, K58, K62, and K63 did not affect binding to procaspase-9, while mutations at Y24, D32, D27, and N73 decreased binding to procaspase-9. See all of the mutations at page 1128.

No Claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Cochrane Carlson, Ph.D. whose telephone number is 571-272-0946. The examiner can normally be reached on 7:00 AM - 4:00 PM, off alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Karen Cochrane Carlson PhD

KAREN COCHRANE CARLSON, PH.D
PRIMARY EXAMINER